IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Chernyshev, Olga N.
Avi ASHKENAZI, et al.	)	Art Unit: 1649
Application Serial No. 09/904,956	)	Confirmation No. 4189
Filed: July 14, 2001	)	Attorney's Docket No. 39780-1618 P2C29
For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**	)	**Customer No. 35489**

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ON APPEAL TO THE BOARD OF PATENT APPEALS AND INTERFERENCES
APPELLANTS' REPLY BRIEF

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

On August 30, 2005, the Examiner made a final rejection to pending Claims 42-46 and 49-51. A Notice of Appeal was filed on November 29, 2005, an Appellants' Appeal Brief was filed February 28, 2006 and an amended Appeal Brief was filed May 30, 2006.

An Examiner's Answer was mailed on June 19, 2006. The following constitutes the Appellants' Reply Brief in response to the Examiner's Answer and is timely filed. This Reply Brief is accompanied by a Request for Oral Hearing.

ARGUMENTS

I. *Claim Rejections Under 35 U.S.C. §101*

Concerning the rejection of Claims 42-46 and 49-51 under 35 U.S.C. §101 as allegedly lacking a specific, substantial and credible asserted utility or a well established utility, in his Answer, the Examiner cites the following arguments:

(1) The Examiner acknowledges that the PRO266 polypeptides cause infiltration of inflammatory cells(s) into the skin of guinea pigs and is generally associated with inflammation (page 8, lines 6-8 of Examiner's Answer), but adds that the instant specification fails to provide any evidence or scientific reasoning to support a conclusion that PRO266 is specifically associated with any specific particular inflammatory disease or condition, including cancer, infection or autoimmune disease (page 8, lines 10-13 of Examiner's Answer). The Examiner concludes that the SVP assay is, at the most, a motivating invitation for further research, experimentation and confirmation as to whether PRO266 is useful as a novel proinflammatory cytokine for treatment of a pathological condition (page 8, lines 16-19 of Examiner's Answer). The Examiner says that 35 U.S.C. §101 clearly states that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention (emphasis added; page 8, lines 19-21 of the Examiner's Answer).

(2) The Examiner does not find the Fong Declaration persuasive allegedly because "there appears to be no record presented in the Declaration or recited in the art that would allow a conclusion that positive testing in SVP assay is predictive of **immediate use** of the testing substance in "enhancing immune cell recruitment to sites of injury or infection or inhibitors to treat autoimmune diseases such as psoriasis." In view of lack of this critical information, the Declaration appears to be limited to Dr. Fong's own conclusions and **no references to scientific reasoning or any evidentiary clinical support** (see Meitzner vs. Mindick, 549 F.2d. 775, 782, 193 USPQ 17, 22 (CCPA 1977), "Argument of counsel cannot take the place of evidence lacking in the record" (emphasis added- page 15, lines 4-12 of the Examiner's Answer).

Arguments

(1) Appellants assertion of utility is based on the positive reaction in the SVP assay (Example 77 in the instant specification), which is well-known in the art as an assay for identifying

inflammatory molecules. This point was discussed in detail in the Declaration by Dr. Sherman Fong, which sets forth the state of the art in the field of inflammation as it existed at the time of the instant filing, and also **presents several exemplary references as scientific evidence** that other assays, similar to the SVP assay, were used for successfully identifying candidate inflammatory molecules.

In this instance, the Examiner herself acknowledges that the PRO266 polypeptides causes infiltration of inflammatory cells(s) and is generally associated with inflammation (see page 8, lines 6-8 of the Examiner's Answer). The art also acknowledges the involvement of proinflammatory molecules in autoimmune diseases and in invasive cancers. In fact, based on the Opdenakker *et al.* reference cited by the Examiner herself, the Examiner adds that, "it is **well described in the art** that **proinflammatory proteins ("molecules") are known to play a key role in the migration of inflammatory cells in autoimmune diseases and in invasive cancers** (page 10, last line to page 11, line 3 of the Examiner's Answer). Thus, based on such teachings in the art, the disclosure of Example 77 within the instant specification (that provides meaningful results for PRO266 polypeptides as a proinflammatory molecule and guidance on how to perform the SVP assay), one skilled in the art would know that PRO266 molecules maybe useful to treat diseases like autoimmune diseases and/or invasive cancers.

Appellants respectfully remind the Examiner that an Applicants' assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "**unless there is a reason for one skilled in threat to question the objective truth of the statement of utility or its scope**." (Emphasis added) *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974). *See also In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. 885 (C.C.P.A. 1980); *In re Irons*, 340 F.2d 974, 144 U.S.P.Q. 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 U.S.P.Q. 209, 212-13 (C.C.P.A. 1977). Compliance with 35 U.S.C. §101 is a question of fact. *Raytheon v. Roper*, 724 F.2d 951, 956, 220 U.S.P.Q. 592, 596 (Fed. Cir. 1983) cert. denied, 469 US 835 (1984). The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the evidence, or "more likely than not" standard. *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). This is stated explicitly in the M.P.E.P.:

> [T]he applicant does not have to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." **Nor must the applicant provide evidence such that it establishes an asserted utility as a matter of statistical certainty**. Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. *M.P.E.P.* at § 2107.02, part VII (2004) (underline emphasis in original, bold emphasis added, internal citations omitted).

The Examiner has the initial burden to offer evidence "that one of ordinary skill in the art would reasonably doubt the asserted utility." (Emphasis added) *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). Only then does the burden shift to the Appellant to provide rebuttal evidence. *Id.* Such a showing has not been made by the Examiner throughout prosecution.

In the Examiner's Answer, the Examiner seems further concerned that "the spectrum of action of proinflammatory molecules are very broad and also dependent on the timing and level of production of a specific proinflammatory protein" (page 11, lines 3-5). In other words, the Examiner's concern is with regard to the underlying mechanism resulting in the positive results of the SVP assay, and not with the result itself.

However, such a rejection is legally incorrect. In fact, the Federal Circuit clearly states that "it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." *In re Cortwright*, 165 F.2d 1353, 1359 (Fed. Cir. 1999). Thus, Appellants submit that such a concern is misplaced, and cannot properly form the basis of a utility rejection.

Even though a proper *prima facie* case has not yet been made for a lack of utility for PRO266, based on the Examiner's own acknowledgement that the PRO266 polypeptides cause infiltration of inflammatory cells(s) and inflammation, the teachings in the art regarding inflammatory molecules and their uses in treating diseases, Appellants believe that they have made a proper case for utility for PRO266 polypeptides in treating specific diseases like autoimmune disease or invasive cancer.

Appellants further submit that while the ultimate use of PRO266 for treating a disease like invasive cancer or autoimmune disease may need further development, case law clearly indicates

that "(t)he mere consideration that further experimentation might be performed to more fully develop the claimed subject matter does not support a finding of lack of utility. For instance, the M.P.E.P. §2107.01 III cites *In re* Brana, 51 F.3d 1560, 34 U.S.P.Q. 2d 1436 (Fed. Cir. 1995) in stating that "Usefulness in patent law....necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is readily to be administered to humans." Further, "to violate §101, the claimed device must be totally incapable of achieving a useful result." *Juicy whip Inc. v. Orange Bang Inc., 51* U.S.P.Q. 2d 1700 (Fed. Cir. 1999), *citing Brooktree corp. v. Advanced Micro devices, Inc.,* 977 F.2d 1555, 1571 (Fed. Cir. 1992).

In other words, utility does not have to be established to an absolute certainty, rather, the evidence must convince a person of skill in the art "to a reasonable probability." Further, the evidence need not be direct, so long as there is a "sufficient correlation" between the tests performed and the asserted utility. Here, there is "sufficient correlation" between a positive result in the SVP assay (*i.e.,* a proinflammatory molecule) and utility in disease conditions like cancer and autoimmune disease.

Taken together, the legal standard for demonstrating utility is a relatively low hurdle. The fact remains that the results of the SVP assay were positive, indicating induction of inflammation. In addition, the Applicant **does not need to provide evidence such that it establishes an asserted utility as a matter of statistical certainty.** Therefore, the Examiner's interpretation of the utility guidelines are incorrect and this rejection should be withdrawn.

(2) As discussed above, the Declaration by Dr. Sherman Fong was presented to set forth the state of the art in the field of inflammation as it existed at the time of the instant filing, and it presented **several exemplary references as scientific evidence** and indicated that several other assays, similar to the SVP assay, were used for identifying candidate inflammatory molecules. The Fong declaration also discussed detailed scientific reasoning, with examples, for using candidate inflammatory molecules for treating diseases like certain inflammatory disease or invasive cancers. Dr. Fong's opinions and the utilities suggested therein, for proinflammatory molecules like PRO266, would readily have been understood, appreciated and accepted by those skilled in

the art at the effective filing date. Moreover, the Federal Court of Appeals held in *In re Alton*, "**(w)e are aware of no reason why opinion evidence relating to a fact issue should not be considered by an Examiner.**" *In re Alton, supra.* Appellants also respectfully draw the Examiner's attention to the Utility Examination Guidelines which state, "Office personnel **must accept an opinion from a qualified expert** that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered" Part IIB, 66 Fed. Reg. 1098 (2001).

Therefore, it is improper to impose this rejection based on an alleged lack of "evidence" in the Fong Declaration. As discussed above, Appellants do not need to provide evidence such that it establishes an asserted utility as a matter of statistical certainty. On the other hand, Appellants need only provide evidence such that it is **more likely than not that a person of skill in the art would be convinced, to a reasonable probability, that the asserted utility is true.**

Accordingly, this rejection of Claims 42-46 and 49-51 should be withdrawn.

II. *Claim Rejections Under 35 U.S.C. §112, First Paragraph- Enablement*

Concerning the rejection of Claims 42-46 and 49-51 under 35 U.S.C. §112, first paragraph, the Examiner indicates that since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

For the reasons discussed above, Appellants submit that the present application sufficiently discloses a substantial, credible and specific utility for the instantly claimed subject matter, and one of skill in the art would know exactly how to use the claimed polypeptides, for instance, in treating diseases such as invasive cancer. Further, the specification provides detailed guidance as to how to identify and make nucleic acids encoding polypeptides having complete amino acid sequence identity to PRO266 polypeptides. The specification also provides ample guidance to allow the skilled artisan to identify those polypeptides which meet the limitations of the claims, found in Example 77 (page 210, lines 22) which describes a dye-based proinflammatory cell infiltration assay in which PRO266 polypeptides induce inflammation, or as "inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the

animal" (page 210, lines 23-24 of the specification). In view of the disclosure within the present application, and the information available in the related field, one of ordinary skill in the art would understand exactly how to make and use the claimed polypeptides without undue experimentation.

Accordingly, this rejection of Claims 42-46 and 49-51 should be withdrawn.

CONCLUSION

For the reasons given above, Appellants submit that the Skin Vascular Permeability assay disclosed in Example 77 of the specification provides at least one asserted specific and substantial patentable utility for the polypeptides claimed in Claims 42-46 and 49-51, and that one of ordinary skill in the art would accept this asserted utility and would know how to make and use the claimed polypeptides. Therefore, Claims 42-46 and 49-51 meet the requirements of 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph. Accordingly, reversal of all the rejections of Claims 42-46 and 49-51 is respectfully requested.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No.**39780-1618 P2C29**).

Respectfully submitted,

Date: August 21, 2006

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